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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,226	01/22/2001	Osamu Ohara	2534USOP	5358

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EXAMINER	
WEGERT, SANDRA L	

ART UNIT	PAPER NUMBER
1647	15

DATE MAILED: 10/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/744,226	OHARA ET AL.
	Examiner	Art Unit
	Sandra Wegert	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-17* is/are pending in the application.

4a) Of the above claim(s) *3-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 January 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The amendment filed 13 June 2003 (Paper No. 13), and the Supplemental Information Disclosure Statement, filed 13 June 2003, have been entered as Papers 13 and 14, respectively. Claim 2 is cancelled. Claims 3-16 were withdrawn by the examiner. Claims 1 and 17 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections and/or Rejections

Title

The objection to the Title, as set forth at p. 3 of the previous Office Action (13 December 2002), is *withdrawn* due to Applicant's amendment correcting the Title (13 June 2003).

Abstract

The objection to the Abstract as set forth at p. 3 of the previous Office Action (13 December 2002), is *withdrawn* because of the amendment which reduced the Abstract to a single paragraph of 150 words or less (13 June 2003).

Claims Objections

The objection to Claim 1 for reciting non-elected subject matter, as set forth at p. 4 of the previous Office Action (13 December 2002), is *withdrawn* because of the amendment which removed references to SEQ ID NO's 3 and 5 (13 June 2003).

Claim Rejections - 35 USC § 112, second paragraph

The rejection of Claim 1 under 35 U.S.C. 112, -second paragraph, as being indefinite for use of the word "substantially," as set forth at pages 12 and 13 of the previous Office Action (13 December 2002), is *withdrawn* due to Applicant's amendment which removed the word "substantially" (13 June 2003) from the claim.

35 USC § 102

The rejection of Claim 2 under 35 U.S.C. 102(b), as set forth at page 12 of the previous Office Action (13 December 2002), is *withdrawn* because of the amendment which canceled Claim 2 (13 June 2003). Remaining and newly-added claims do not recite "a partial peptide."

Maintained Objections and/or Rejections

Sequence Rules

The objection to the instant application for not being in compliance with the sequence rules, as set forth at p. 3 of the previous Office Action (13 December 2002), is *maintained.* Applicants are required to amend Figures 1, 2, 4, 5 and 7-24 to insert the appropriate SEQ ID NO for each peptide or nucleotide sequence listed (see 37 CFR 1.821-1.825).

35 U.S.C. § 101/112, first paragraph-, Lack of Utility, Enablement.

Claims 1 and 17 are rejected under 35 U.S.C. 101, as lacking utility. The reasons for this rejection under *35 U.S.C. § 101* are set forth for Claims 1 and 2 at pp. 4-11 of the previous Office

Action (Paper No. 11, 13 December 2002). Claims 1 and 17 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth in the previous Office Action (Paper No. 11, 13 December 2002), one skilled in the art clearly would not know how to use the claimed invention.

The claims are directed to a polypeptide that possesses approximately 80-95% homology to latrophilin receptors such as bovine LTX-3 (Matsushita, et al, 2000, Accession No. T18389) and rat *CL3AA* protein (Sugita, et al, 2000, Accession No. T17186). As discussed in the previous Office Action (p. 5), no well-established utility exists for newly isolated complex biological molecules. The specification does not disclose experiments that impart *any* function for the putative receptor polypeptide encoded by the claimed nucleotide in the context of the cell or organism. The specification does not teach the skilled artisan how to use the receptor peptide for any unique or specific purpose. For example, there is no disclosure of the use of ligands of the receptor, or changes in the physiology of transfected cells, or the phenotypes of "knock-in" or "knock-out" organisms, or of second-messenger assays, or of diseases caused by an overactivity or underactivity of the receptor. The skilled artisan is not provided with sufficient guidance to use the claimed polypeptide for any specific and unique purpose.

Applicants argue (page 6, for example, 13 June 2003) that the polypeptide of the instant Specification is a G-protein coupled receptor, and that homology of the disclosed polypeptide with a class of proteins already having utility shall impart sufficient utility on the novel polypeptide and on the polynucleotide encoding it. However, the polypeptide of the Instant Specification and the polynucleotide encoding are unidentified molecules. The polypeptide

possesses moderate homology to known G-protein coupled receptors-- for example: rat *CL3AA* protein, which *itself* is uncharacterized as to a function within the organism (Sugita, et al, 2000, Accession No. T17186).

Applicants further argue against the Utility/Enablement rejection by discussing the usefulness of receptor proteins as pharmacological targets (p. 7, third paragraph, 13 June 2003), arguing that the "expressed polypeptide of the claimed invention is easily adapted to methods well known in the art for screening for ligand/antagonist activity" and that "the selection of specific compounds for testing in the asserted screening assay is not required as that is not a specific element of the claimed invention" (page 7 third paragraph, 13 June 2003). In fact, specific pharmacological data is one example among many given in the previous Office Action (13 December 2002) of the type of evidence that would serve to enable the instant invention. There are many types of evidence or data *specific* to the receptor of SEQ ID NO: 1 that would enable the claimed invention. For example, an enabling disclosure might identify ligands which bind specifically to the Applicants' GPCR and then give evidence of receptor transduction after agonist binding, or it might discuss changes in the physiology of *knock-in* or *knock-out* animals, or it might identify a disease caused by the mutated receptor of SEQ ID NO: 1, etc.

Despite the Applicant's arguments (p. 7, second paragraph, 6 June 2003) there is no evidence that the protein disclosed in the instant Specification functions as a G-protein coupled receptor. However, even if it were established as such, additional specific functional assays would be needed since this family of proteins is very large and enormously varied (Ji, et al, 1998, JBC, 273:17299). Even closely-related family members sometimes work very differently and have different specific functions in the organism (Ji, et al, 1998, p. 17302, 3rd paragraph). While

it is true that GPCR proteins have some structural features in common, this family of transmembrane receptors is noticeable for its *lack* of high homology of amino acid sequence (Probst, et al, 1992, DNA and Cell Biol., 11:1-20; Joost and Methner, 2002, Genome Biology, 3(11): 1-16)—except, for example, in membrane spanning α-helices where the amino acid composition is constrained by hydrophobic forces (Probst, et al, 1992, DNA and Cell Biol., 11:1-20). Agonist binding sites, for example, show very low percent correspondence (Probst, et al, 1992, DNA and Cell Biol., 11:1-20, Fig. 2, page 4). And, despite the fact that intracellular transduction mechanisms converge (e.g., binding of only a limited numbers of G-proteins), the intracellular binding sites also bear very low homology (Probst, et al, 1992, DNA and Cell Biol., 11:1-20, Fig 2, pages 8 and 9; Joost and Methner, 2002, Genome Biology, 3(11): 1-16, Figure 1).

One skilled in the art would not know the utility and function of the polypeptide disclosed in the instant disclosure, even if it *were* a G-protein coupled receptor because, as discussed in the related art above and in the Specification of the instant application (pp. 1-2), G-protein-coupled receptors are "present at various functional cell surfaces" (page 1, third paragraph) and mediate numerous physiological functions.

It was noticed that "EST's" (expressed sequence tags) were referred to throughout the Applicant's response (13 June 2003; pages 6-8, multiple references). EST's are randomly-generated short pieces of cDNA that are unique to a gene (although many genes are represented by multiple EST's). However, they give little information as to the function of a gene (see: Wolfsberg and Landsman, 1997, Nucleic Acid Res., 25(8): 1626-1632). Since EST's

were not discussed in the Office Action of 13 December 2002, it is not known why they were mentioned as a point of comparison when discussing the function of the Applicant's claimed receptor.

New Objections and/or Rejections

35 USC § 112, first paragraph – Written Description.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claim 17 is directed to a protein of SEQ ID NO: 1, in which 1 to 30 amino acids are deleted, added or substituted.

The specification teaches the protein of SEQ ID NO: 1. However, the specification does not teach functional or structural characteristics of the protein of SEQ ID NO: 1 in which 1 to 30 amino acids are deleted, added or substituted. The description of the protein of SEQ ID NO: 1, in which 1 to 30 amino acids are deleted, added or substituted, and described only as having the same activity as the protein of SEQ ID NO: 1, is not adequate written description of an entire genus of functionally equivalent receptor proteins.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at

page 1116).

With the exception of the protein of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed proteins, and therefore would not know how to make or use them. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of making or using. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use: *The product itself is required.* See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the protein of SEQ ID NO: 1, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 9:30 AM to 6:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SLW

10/15/03

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER